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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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DISEASES of the NERVOUS SYSTEM

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A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

The Etiological Significance of Contrast Media in Post Lobotomy Complications

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Hartford, Connecticut

Efforts directed towards retraining and rehabilitation of patients following lobotomy operations were noted to be significantly retarded, in a large number of patients, by the presence of postoperative involvement of the lower extremities, apparent stiffness of the back and general reluctance on the part of these patients to move about. At times, they actively resisted efforts to have them participate in the program designed for their maximum rehabilitation. These findings have been previously noted by Marcovich et al[1] and Ziegler and Osgood,[3] but the etiological conclusions were equivocal. This report is based upon the findings that resulted from an investigation stimulated by the desire to obviate these difficulties rather than any particular interest in neurological research. The findings do, however, suggest that further study and investigation of them could result in further knowledge of cerebral function, by possibly removing that area as the origin of these postoperative complications. Also, to obviate or diminish these complications might shorten the postoperative period of extreme lethargy and inactivity, and permit an earlier evaluation of the results and a more prompt beginning of the retraining program.

This report is admittedly incomplete, because of the insurmountable difficulties associated with determining the exact brand and type of contact media or the exact amount of media used. Also a well delineated syndrome resulting from the use of such material has not been established. The few reports noted were concerned with spinal myelography studies.

The objection that an insufficient number of lobotomies have been studied can be met only by the remark that a similar number of cases in which such a large amount of media had been used is probably not available and should never be. In spite of these handicaps, this comparative study seems at least provocative and worthy of further consideration by those interested in both lobotomies and the study of neurological localization.

The study began as a result of frequent reports about post-lobotomy patients, received from the nursing departments of "stiff back," "difficulty in walking," "trouble bending over" and "slow, awkward movement" that strangely disappeared or seemed minimal when investigated by the doctors in charge. This apparent inconsistency was later found to be a result of improvement under physical activity. These reports were further studied and it was found that objective evidence of these manifestations had been noted as early as ten (10) days postoperative, and as late as four (4) months postoperatively. Generally, the onset has been noted two weeks postoperatively, and definite improvement was apparent approximately five weeks later. Only one case had signs which continued

*From The Institute of Living.

longer than 2½ months postoperatively. For this investigation all patients were studied for signs present during the first postoperative month (See Chart 1).

The following is a report requested of a specially trained psychiatric aide who was assigned to the same patient each day to facilitate the training program—the report seemed particularly observant and gives quite a clear picture of the clinical findings frequently encountered in lobotomized patients which either slowed or seriously impeded their progress of retraining.

Case 1: (4 months postoperatively).

"In the morning when the guest awakens she is usually stretched and rigid, even up to her neck. She likes to have both legs swung off the bed, then she pushes herself up. Will respond 'yes' if asked if her legs hurt and once shrank and said 'ouch' when her weight was first put on feet, and ankles bent. She will walk on her toes, touching aide or walls for balance, and goes up the bathroom steps bearing her weight on left leg only, swinging the right one around as if stiff. Undresses and climbs in tub gingerly, may groan or sob a little as she gets into water, squatting in it for quite awhile. She gets up and out without assistance, drying legs tenderly (if at all) as if even the skin were tender. Sometimes she will put her foot or leg into a desired position with her hands. Throughout the morning, and less noticeably in the afternoon, she sits down as if one leg (right) were stiff, climbs the stairs with effort, or stands on her toes...."

CHART 1

	Edema Lower Extremity	Bullae	Resistive to Movement	Stiff Back	Prolonged Lethargy
GROUP A					
1.	4 plus*	bilat.	marked	mild**	marked†
2.	4 plus	bilat.	marked	marked	marked
3.	2 plus	unilat.	mild	marked	mild
4.	1 plus	none	mild	none	mild
5.	1 plus	none	mild	none	mild
6.	4 plus	bilat.	marked	marked	marked
GROUP B					
1.	none	none	none	none	none
2.	none	none	none	none	none
3.	none	none	none	none	none
4.	none	none	none	none	none
5.	none	none	none	none	none
6.	none	none	none	none	none

Group A—contrast media used at time of lobotomy.
Group B—no contrast media used.
*Plus indication of edema according to usual clinical estimate of degree.
**Mild indicates objective evidence but not sufficient to retard retraining.
†Marked indicates degree sufficient to retard retraining.

The examination of this patient revealed slight mottling of the skin, minimal edema over the tibia bilaterally, her gait was slow and deliberate, but there was no evidence of incoordination. The deep reflexes were plus two and symmetrical and no patholigical reflexes were elicited. With leading questions, she was able to give a history of subjective pain, deep along the anterolateral aspect of the right thigh. It was noted that the patient would tend to remain in a rather rigid sitting position for prolonged periods unless she was continuously urged to participate in the active program outlined for her.

Early in this investigation, it was noted that the other patients who were affected by postoperative complications of (1) lower extremity edema, (2) back stiffness, (3) reluctance to engage in physical activity as a result of difficulty in locomotion, or showed reluctance to move about because of apparent tenderness of pain in trunk or lower extremities, had in every case an accumulation of contrast media in the caudal sac. This accumulation varied in amount but appeared to be between 4 and 8 cc. in the sac with variable amounts which had migrated along the peripheral nerves of that region. Later it was found that immediately after the lobotomy the media is freely movable in the areas ordinarily occupied by cerebrospinal fluid in the vertebral canal.

After an individually variable length of time, the media becomes fixed in the caudal sac and along the peripheral nerves. The relationship of this free motion of the media to the horizontal sleeping position can be readily correlated with both the early morning exaggeration of the complications and the frequent transitory manifestations at levels above the ultimate position assumed by the media in the caudal sac. After personal communications with various neurosurgeons and neurologists and a study of the recent literature was made, the following observations were revealed:

1. The presence of the contrast media in the caudal sac following lobotomy was well known, but it had been considered of little or no importance.

2. Previous studies specifically relative to contrast media had revealed:

A. The effects of the presence of the media in the caudal sac following spinal myelography were not uniformly agreed upon. Previous studies were of little value for the present study, as the cases cited had had lower extremity signs or symptoms prior to myelographic study[1]. Although no specific uniform syndrome resulting from contrast media remaining in the caudal sac could be determined, the use of contrast media for spinal myelography was considered to be a procedure requiring considerable deliberation and caution.

B. One rather well done study by Boldray and Aird,[2] which was based on experimental evidence, revealed that, without significant differences, as to the type of contrast media available at that time, the property of being definitely irritating to the meninges was shared by them all. It was of particular interest to this study that it was demonstrated that the amount of meningeal irritation was proportional to the amount of contrast media used. As an additional factor it was noted that the presence of free blood in the experimental field increased the amount of meningeal irritation.

C. The admonition to use a maximum of 3 or 4 cc., and to always remove the media after x-ray studies was frequently noted.

The following excerpt from a report by Tarlov[7] of a case complicated by the use of iodized oil seemed typical:

"From the present case and a survey of the literature there is no doubt that an inflammatory and proliferative meningeal reaction may follow the intrathecal introduction of pantopaque. It should be restricted, therefore, to those cases in which critical information is urgently needed for diagnosis and treatment. When employed it should be injected immediately before fluoroscopy is done and it should be removed immediately after the myelography."

However, even after extensive searching of the literature, no reason for such an admonition, sufficiently established for conclusive purposes, could be found. The literature concerned with post-spinal myelographic study complications associated with the use of iodized poppy seed oil was literally rife with studies of single or small series of cases which showed the possible harmful effect of the media. Because of such reports, a large series of cases were carefully surveyed by Marcovich et al[1] and this study minimized the dangers.

Bucy,[5] some 18 months later reported:

"In our experience the intraspinal use of iodized oil has been so innocuous that one of us (P.C.B.) has repeatedly expressed the opinion that its use was not associated with any permanent undesirable effects and that in those few instances in the literature in which development of symptoms were attributed to the use of iodized oil the case against the oil had by no means been established. Furthermore, the study[1] substantiated that opinion. Accordingly when the present case came under our observation and when the operation and postoperative course seemed definitely to establish the relationship of the iodized poppy seed oil to the development of symptoms of the spinal cord, we thought it necessary to report the case in detail."

This case showed "weakness of both lower extremities, progressive stiffness to such an extent that it became difficult for him to get about without using the walls and furniture for support, lower extremity numbness, burning pain along medial aspect of the right foot and severe extensor spasticity, hyperactive tendon reflexes, ankle clonus and bilateral Babinski."

All of these findings disappeared after the removal of iodized oil. The similarity of these symptoms with those of the cases reported herein are very striking. It is of little surprise that it is difficult to evaluate the etiology as the effects of proven arachnoiditis of the spinal canal, not associated with iodized oil, also are quite varied as shown in a study of this subject by French[6] who found considerable variation as to etiology, location, pathologic process, individual response and clinical course.

3. The study by Ziegler and Osgood[3] was concerned with complications following lobotomy but had not emphasized the feature (contrast media) under consideration in this paper.

Their study of a significant number of cases was primarily directed towards the investigation of complications similar to the ones considered in this investigation. In their series approximately 40 per cent had lower extremity complications. In the article it was

noted they "customarily used iodized poppy seed oil" but the cases were not distinguished on the basis of having had the oil used.

Zeigler and Osgood[3] concluded:

"We have not satisfactorily explained clinical complications in lower extremities in case of post-lobotomies, however, bedside observation and experimental investigation point to areas in brain, lesions of which may produce edema and vascular and trophic disturbances."

Any reliable conclusion would of necessity have to meet the obvious objection that many cases which had had contrast media used had not been noted to have similar complications. In their work concerned with similar complications, roughly 60 per cent were shown not to have had these complications. The cases presented had not been divided by the criteria used in this investigation, and it was only noted that contrast media had been "customarily used." A possible reason that only 40 per cent had similar complications, such as those noted in this study, was that seldom was more than 1 cc. used. This amount seems less likely to cause as much arachnoitis and subsequent minimal edema which could well have been overlooked. The study prior to that time by Kendwall[4] had revealed:

"One complication that we have observed in several of our cases, with varying degrees of completeness. This consisted of edema, blister formation, and sometimes tenderness and pain in one or both feet or legs. These signs usually appear during the month following lobotomy. One of these symptoms may run alone or with one or both of the others. The commonest is the pitting edema, which is bilateral and sometimes symmetrical: We believe that this is a trophic disturbance secondary to the surgical leison."

General Consideration

The selection of patients for this study was based only on their being in residence at the time of the study in order to permit personal observation of the patients used for the investigation. Six patients had had contrast media used at the time of their lobotomy and a similar number was selected, alphabetically, in which the contrast had not been used. Of significance for valid comparative study, those not having contrast media used had also been subjected to a different surgical technique. Four different neurosurgeons had been the operators; two had used iodized poppy seed oil and two had not. This investigation began without preconceived ideas, solely because Dr. C. C. Burlingame assigned to the writer the job of determining the nature, and, if possible, the cause of the "stiff backs" which were reported by the nursing personnel. All judgments in regard to the involvement of symptoms have been made solely by the writer. At the onset of the study the writer was not aware that iodized oil had been used or that it was in any way relative to the symptoms. The accumulation of the oil in the caudal sac was noted quite incidentally when x-ray examination was requested for "the whole skeletal system from skull down" in a pessimistic search for "any pathology" that would account for the symptoms in case number one.

In all the cases the complications had been previously noted and recorded by other staff doctors, except the two more recently lobotomized patients which were examined by the writer. The findings of the latter were checked and confirmed by three competent men. Figure 1 is an x-ray of Case 1 taken four months postoperatively which was reported as follows:

X-ray report, Case 1, taken Nov. 4, 1947.

Comment: AP and lateral films of the lumbar spine, sacrum and pelvis reveal approximately 2 cc. of contrast material (pantopaque) free within the sacral canal, a similar amount fans out along the sacral root sheath. This is slightly more marked on the right side where the oil is noted anteriorily as far as the sacrosciatic notch.

Impression: Approximately 2 cc. of contrast media within the sacral canal with similar volume extra durally located paralleling the sacral nerves as far anteriorily as the sacro scialic notch on the right.

Figures 2 and 3 are x-rays of Case 2, taken 22 days postoperatively. The neurosurgeon had reported that 3 cc. of contrast media had been used. These figures show, in addition to the rather dramatic appearance; the difficulty of accurate study concerned with the amount actually used and the amount reported to have been used. X-ray report on Case 2, figures 2 and 3, 22 days postoperative on November 6, 1947 was as follows:

Comment: AP and lateral films of the lumbar-sacral spine and pelvis revealed approximately 8 or 10 cc. of free material (probably pantopaque judging from its appearance) within the lumbar spinal canal. This readily flows from L 2 to the caudal sac. There is, in addition, less than 1 cc.,

Figure 1

Figure 2

Figure 3

subdural in location and paralleling the sacral nerves sheaths. Nothing further of significance is noted. (The apparent kinking seen on lateral film was shown to be an artefact by the appearance on subsequent projections).

Impression: Approximately 8 to 10 cc. of contrast material (Pantopaque) within lumbar spinal canal. Multiple droplets parallel in the sacral nerves, subdural in position. (This showed the rapid accumulation of the media in caudal sac and its progression along the nerves).

Neurological consultation revealed "sluggish body movements, upper extremities normal, abdominal, cremasteric, knee jerk and ankle jerk present and hyperactive. No Babinski or ankle clonus. He can move the right leg normally, but he will not lift left leg or flex it on abdomen. When he attempts to move left legs, a coarse tremor of entire left leg sets in and then stops. The skin of the entire leg, thigh and foot is warm and dry while that of the right is cold and moist. There is a large intact blister over the left heel. I believe that the condition of the patient's trunk and left leg movements and sympathetic changes are central in origin."

By comparison with Figure No. 1, taken 4 months postoperatively, the relative lack of absorption over period of months is noted. This residual oil, with relative clearing of symptoms, suggest several possibilities. The most obvious one is that the current consensus of opinion which minimizes the finding, is not justified, as the experimental work[2] and the present study suggested strongly that the contrast media acts both as an irritant and as a space occupying mass. Apparently the normal forces of resistance overcome the irritation of the meninges and is followed by reduction of manifestations or arachnoiditis with remission of symptoms in most cases. The stoic, relatively insensitive, lobotomized individual is very unsatisfactory for the study of subjective pain and tenderness. The clearing up of the obvious edema, etc., in the light of Case 1, suggests that previous observations, i.e. "that the symptoms disappear after a short while," were unduly optimistic. The present study revealed that two or more of the following findings; edema of both lower extremities, reluctance to engage in physical activity, bullae of the feet, prolonged lethargic state, and stiffness of back, as evidenced by reluctance to bend from trunk, and arising from sitting position in a stiff awkward fashion, were present in all of the cases in which contrast media had been used. A similar number of cases in which

it had not been used are shown for comparison in Chart 1. None of these complications had been noted in this group.

This comparison is not valid for conclusive purposes as to the role of the contrast media as a different surgical technique (Leyerly) had been used in those cases which had not received contrast media, whereas the standard lateral (Watts and Freeman) approach had been used in the cases in which the media had been used. The most obvious implication is that either the media itself or the surgical approach is responsible. The startling radiographic pictures of (and the irritating foreign body and space occupying nature of the media) in the caudal sac, along with the distance of the surgical field from the sensory and motor areas would tend to minimize the surgery per se. This neurosurgical consideration must, however, be passed upon by more qualified investigators.

A brief study of Chart 1 is certainly sufficient to indicate the need for further and more comprehensive study to definitely determine the etiology of the complication—fortunately, and possibly accounting for the previous lack of interest, the complications do generally diminish. If, however, it should be established that these findings were directly related to the foreign body in the caudal sac, some rather nebulous neurological implications could be dismissed from further consideration as the origin of the complications. In addition the near hypothetical discomfort to the patient could be removed and speed up the retraining program.

Any reliable conclusion would of necessity have to meet the objection that many cases which had had contrast media used had not been noted to have similar complication. The most probable reason is that only seldom has more than 1 cc. been used. This amount apparently is less likely to cause as much arachmoitis and any subsequent minimal edema could well have been overlooked. The lobotomized patient rarely complains and the edema frequently existed for a relatively short periods, even in the cases studied herein.

The complication usually did not appear until after the patient returned to the psychiatric service for retraining where the patient was followed less closely and the complications not likely to be seen by the neurosurgeons.

Summary

In a series of twelve (12) cases, half of whom had had contrast media used at the time of the lobotomy, were studied for any possible relationship between the use of the oil and post-lobotomy complications. From this study, it would appear that there is a direct relationship between the media and such complications, but the variables were such that no conclusive statement could be made as to the relationship.

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*Electroshock Therapy in Neurodermatitis**

(CASE REPORT)

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Fort Logan, Colorado

Although Bauer and Perrin[1] reported "dramatic improvement of skin lesions" in psychotic patients given electroconvulsive therapy, there has been no mention of treatment of neurodermatitis by use of such therapy in a non-psychotic patient.

The following is an interesting case of severe generalized, recurrent neurodermatitis in a sensitive, neurotic personality of bright normal intelligence, who failed to respond to practically every known medication.

Case Report

This 24 year old white male was first admitted to the Veterans Administration Hospital, Fort Logan, Colorado, on August 21, 1947, complaining of a generalized itching, weeping, exfoliative dermatitis. Dysidrotic lesions of the fingers were noted, with some cracking and regeneration of the nail substances. His temperature was 99 degrees F. Except for the dermatitis, physical examination was negative, although the patient appeared very tense, anxious and irritable. He had been treated on several occasions since 1946 at the Veterans Administration Hospital, Dallas, Texas, for a chronic skin condition dating to service in the Navy. While he was at sea for almost three years he noticed that an eruption would appear in the antecubital fossa of the left arm but tended to become quiescent. When the patient returned to the United States and began to wear woolens, the eruption appeared and was more lasting and more annoying. Following his discharge from the Navy it became more generalized. The first hospitalization was July 4, 1946 when a diagnosis of neurodermatitis was made; he improved sufficiently to be discharged in September but again required hospitalization for one month in December 1947.

Flare-ups of the dermatitis were believed to be correlated with emotional upsets and within a few hours after a family argument there was increase in erythemia of the skin with itching, weeping, scaling and cracking of the skin following in that order. The scalp, palms and soles of the feet were involved; only the penis and scrotum seemed to be spared from the malady.

Laboratory examinations were negative, including complete blood count, urinalysis, blood serelogy, blood cholesterol and BMR. A skin biopsy was reported as showing "chronic neurodermatitis," and a lymph node biopsy (axillary) was reported to show only "chronic inflammation."

It was the opinion of the psychiatrist that the patient showed a moderate anxiety state, and a Rorschach test confirmed this impression. He was treated with sub-shock insulin with much improvement in the dermatitis; however, the insulin treatments were discontinued after ten days because of "adverse reactions." It was recommended that the patient have a "change to a cool climate" and consequently he was transferred to the Veterans Administration Hospital, Fort Logan, Colorado.

On the first admission to Ft. Logan he received practically every type of known dermatological treatment, including various colloidal baths, ultraviolet light, applications of oils, cremes and ointments, soaks to the skin, auto-injections of blood into the gluteal muscles, and intravenous calcium gluconate. Crude liver injections, vitamins and low fat diet appeared to give no alteration in the dermatitis. An allergic survey showed sensitivity to several foods. In view of an eosinophilia of 12 per cent, Rowe's elimination diet was prescribed as it was believed that there might possibly be an allergic basis for the ailment. By the time of discharge on December 16, 1947 a regular diet was being given and the patient was in evident remission from the dermatitis.

He returned to his home in Texas, but on

*From the Medical Service, Veterans Administration Hospital, Fort Logan, Colorado.
Authors' Note: Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

December 19, 1947 was again admitted to the Veterans Administration Hospital, Dallas, Texas, because of acute recurrence of his difficulties. Apparently there had been some conflict with his family. He made gradual improvement on mild compresses and soaks, plus mild sedation. The exacerbations were noticed each time the patient went home on a short pass. He was transferred to Ft. Logan for the second time on February 5, 1948, complaining bitterly of his dermatitis. Again he was treated with a multitude of lotions, compresses, baths, auto-injections, penicillin, anti-histamine drugs, etc. He was placed on a pure protein hydrolysate diet for a week with no visible change in the skin condition. A biopsy of an inguinal node was reported as showing "fibrosis, cause undetermined." During the hospitalization it was strikingly evident that any new form of therapy would give improvement for a short time and then the patient would relapse to his previous condition. No therapeutic agent ever offered any permanent beneficial effect.

Finally the patient was seen by the attending neuropsychiatrist, who recommended electroshock therapy, as it was noted that there had been a tendency to improve on previous insulin sub-shock therapy. Six electroshock treatments were given culminating each time in a grand mal reaction. Curare was given prior to each treatment and no complications resulted from the therapy. The dermatitis improved markedly although it could not be immediately concluded that electroshock therapy gave permanent relief. The patient was anxious to return home and he was discharged on May 28 with a final diagnosis of "neurodermatitis disseminata." He was instructed to keep his skin lubricated with mineral oil or vaseline as needed and to avoid exposure to sunlight as much as possible.

Summary of the laboratory data of the first admission at Ft. Logan reveals negative findings except during the episode of pneumonia in December 1947; however, there has been a transient eosinophilia and a moderate elevated sedimentation rate has existed. Chest x-ray films have been negative except for pneumonia of the right lower lobe in December 1947.

The patient seemed to be doing fairly well until June 30, 1948, when he again became very ill and required hospitalization at the Veterans Administration Hospital, Temple, Texas. The dermatitis was about as described previously; general physical condition was good. Laboratory data at Temple, including CBC, urinalysis and blood serology were negative. Sedimentation rate was 17 mm. per hour. He received various combinations of ointment and compresses, but obtained relief only after being placed in an air-conditioned ward. The dermatitis, however, remained acute and it was recommended that he be sent to Ft. Logan.

The patient was readmitted to Ft. Logan Hospital on August 3, 1948, suffering from the dermatitis which was generalized and erythematous, but not weeping. Otherwise there was no change in the physical condition. He asked to be given electroshock therapy, as he volunteered "the shock treatments are the only things that help me."

Shortly after the third admission the patient had an argument with a fellow patient and almost immediately became highly nervous, upset and irritable, and soon he had a full blown, generalized, weeping, dermatitis condition which could be described the severest episode he had had. It was necessary to sedate him heavily with sodium amytal. The attending neuropsychiatrist began a series of electroshock treatments on August 9, and a total of 13 convulsions of a grand mal type resulted, the treatments being given twice weekly until September 8. Laboratory data has shown no appreciable changes as compared to those of previous admissions.

After the second convulsive treatment, the dermatitis subsided amazingly and by the end of the fifth treatment, the condition appeared only as a dry, mild, excoriation, and the patient was able to take full active part in recreational activities.

During hospitalization the patient was given numerous psychological tests completed before the electroconvulsive therapy was begun. He was very cooperative throughout the examinations and achieved an intelligence rating of "bright, normal" on the Wechsler-Bellevue scale. The scatter pattern suggested neurotic anxiety, but no specific clinical group. The Rorschach indicated good contact with reality. Analysis of the quantitative and qualitative aspects of the records suggested phobic personality, with immature obsessive

phantasy formation in a sensitive, somewhat passive individual. The responses in the sentence completion test reinforced the impression of passivity in this individual despite a high level of aspiration. Feelings of not being appreciated by others and possible guilt feelings were indicated. The summary of these tests were therefore revealing of sensitive, over pliant phobic personality in an individual of bright, normal intelligence.

The patient has been afebrile since August 27th, whereas prior to the institution of electroshock therapy, at times had had a fever to 99.2 degrees F. He was also examined regularly by the attending dermatologist who noted the continued improvement. The patient was given staphylococcus toxoid twice weekly intradermally to control the secondarily infected excoriations and was given psychotherapy between the administrations of electroconvulsive therapy.

Comment

The case presented is of particular interest inasmuch as a non-psychotic patient with a severe neurodermatitis has not, to our knowledge, been treated previously with electroconvulsive therapy. We have been unable to find a similar case reported in the literature, although one article mentions improvement of dermatitis in psychotic patients given electroconvulsive therapy specifically for the psychosis.

Although the case we have presented benefited greatly from the electroconvulsive therapy, the prognosis remains guarded. However, we can definitely state that the shock therapy has given better results than any other type of therapy we have attempted on this patient.

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Personality Mutation Following Carbon Dioxide Inhalation

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Sacerdotal healing - disciplines, predominantly psychological in their therapeutic modalities, have been of sufficient repute to gain and hold the eye of history from antiquity to the very present. No age, no culture has lacked for multiformulations of human essence. Throughout what might be informally called the medico-sacerdotal era of psychiatry, there is copious historical evidence of the pendulating weight of emphasis, causatively considered, on either the somatic or the psychic component of human illness. For instance, things psychiatric went definitely anatomical, physiological, histological, and bacteriological during the age of "pure science"—a nomenclature-crazy era wherein the nonformularistic was deemed scientifically unworthy, and the immeasurable was shrugged off as inconsistent with actuality, as adjudged by the contemporary "mind," which was "a mysterious form of matter secreted by the brains," and whose chief activity was considered to consist "in the endeavor to ascertain its own nature, the futility of the attempt being due to the fact that it" (had) "nothing but itself to know itself with.[1]" Indeed the confusion of the "mind" with the "soul" and the quasi-controversial dichotomy of psyche and soma probably still persists to considerable degree in the practice of general medicine if not in its theory. In the field of psychiatry, and with more than a hint of neo-sacerdotalism, the last century saw the pendulum swing in an arc almost eliminative to the organic pole of psycho-somatic relationship.

In retrospect, medical men (but not "medicine men") have found it easy to accept the physical causation for "mental" ills, while the converse idea was not well entertained until the meshing of socio-anthropological, of psycho-pedigogical, and of freudian principles, which resulted in a dynamic concept of personality in terms currently known as

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psychophysiological functions. So right now the pendulum seems to be in fairly comfortable mid-swing. But the swirl of discovery agitated by inferential speculation soon may make the profundity of today the bathos of tomorrow.

Invitational to speculative thought along these inter-relational lines, is Meduna's[2-4] rather recently introduced Carbon Dioxide Inhalation Therapy. In the inventor's and others' hands[5,6] as well as in the experience of this author this therapy has been productive of startling immediate intermissive behavior during its application, and has been followed by personality mutation of more or less propitious clinical consequence. After about two years of its clinical use, first in the recommended field of the psychoneuroses as well as in the treatment of character and behavior disorders, and later on during the remission-interval of the psychoses, the author's own observations of the physiological, the psychosensory, the psychomotor, and the psychological manifestations as well, agree with initial and current reportings. Our clinical results in the main, have met the claims made for the method. However, the author's conclusions concerning its mode of operation are somewhat at variance with the several reported opinions that have come to notice.

Historical

In 1929 Leake and Waters[7] reported the safe narcotization of animals with various CO_2-O_2 mixtures up to 80 per cent—20 per cent without increasing the CO_2-content of the blood above 65 volumes per cent over short intervals of inhalation; relatively short application of pure carbon dioxide brought about a fall in blood pressure, with simultaneous arrest of heart and respiration with consistent resumption of same following prompt insufflation of oxygen.

In 1912, Verworn[8] theorized that general anaesthesia consists essentially of reduced oxygen fixation or absorption in the cells of the nervous system. However, six other theories[9] of general anaesthesia have continued to merit recognition. Despite this erudite contention general anaesthesia has managed to remain useful for over a century.

In 1916 Loevenhart *et al*[10] while working on the relations between oxygen-fixation and the respiratory center, injected a dementia precox patient intravenously with a 0.1 per cent solution of sodium cyanide and, incidentally, it was observed that catatonic muteness of several months' duration disappeared for a short time. Ten years later, a directed study[11] proved the predictability of what the above researchers called "psychic stimulation" by the cyanide solution. Subsequently a switch was made in favor of an inhaled mixture of CO_2-O_2 in proportions of 10:90 to 40:60 with similar results on psychotic subjects; higher concentrations of CO_2 were administered with caution and without untoward effect. It was deduced by them that the mechanism producing the temporary verbal contact was a "psychic stimulation," a "cerebral stimulation," a "stimulation of the cortex" (the terms were seemingly applied indiscriminately) — such "stimulation" being considered identical with that activating the medulla, and to be of an oxidative metabolic nature. Loevenhart *et al* further asserted[11] that the reported temporary restoration of mental function was brought about by the application of sufficient increase of CO_2-volume to the cerebral cells psychopathologically less irritable to a normal carbon dioxide blood content. The physiology of the day had it that depending upon the state of the cell, on the basis of time-lag between the disturbance, of (a) *aerobic* oxidative cell metabolism, and the (b) *anaerobic* oxidative cell metabolism, an abruptly managed decrease in oxygen-fixation might induce transient stimulation of the cell. This was claimed as accomplished by massive carbon dioxide administration, and six "levels" of oxygen-fixation with their functional expectancy (in terms of "psychic depression" or "psychic activity") were described. Roseman *et al*[12] in 1945 induced and quantitatively evaluated rapid changes in cerebral oxygen tension by varying the oxygenation and circulation of the blood.

In 1947 Meduna[2] after reinvestigation confirmed the conclusion of Lovenhart *et al*[11] concerning the absence of lasting effect of carbon dioxide inhalation in any psychotic condition. Further he postulates that the apparent inefficacy of other than cortically induced epileptogenic therapy in management of psychoses supports the belief that schizophrenias, schizophreniform states, mel-

ancholias, etc., are disturbances of cortical function, whereas psychoneuroses are conceivably concerned with lower structures which have to do with emotional evaluation.

Confining his subsequent reportings to the latter type of disorder and with studied minimization of inter-communicative psychotherapy, Meduna devised a treatment technique of CO_2-O_2 treatment-mixture inhalations, reporting encouraging results in all but the anankastic reactions. Four phases[2-4] of physiological reaction to the carbon dioxide administration are described: (a) subcortical excitation, (b) cortical inhibition, (c) psychomotor and psychosensory excitation possibly by the stimulated subcortical structures, and (d) extra pyramidal and other motor phenomena, and subcortical epileptiform attack.

In the *first phase* Meduna describes abrupt increase in respiratory and pulse rate, elevation of peripheral blood pressure, dilation of the pupils, flushing and sweating; he ascribes this to "subcortical irritation." The onset of narcosis is considered to initiate the *second phase;* this, he considers, the result of "cortical inhibition." "Psychomotor and psychosensory excitation" are designated as characterizing the *third phase* and stimulation of the subcortical structures is the suggested cause. With continued inhalation of the CO_2-O_2, Meduna describes the successive appearance of slight tremor, tetanoid spasms of the hands later spreading to the face or trunk, athetoid movements, ballism, rigidity first of the flexor, later of the extensor muscles, Babinsky sign, decerebrate rigidity, and finally, upon withdrawal of the agent, epileptiform attacks; this syndrome he considers to be extra pyramidal and the other motor phenomena as well as the convulsions were designated as subcortical in origin and, for the reasons stated above, of limited therapeutic significance.

Meduna's preliminary report on 38 cases, contained the belief that his treatment would prove salutary in a wide range of functional behavior disorders, because it constituted a direct physiological approach to the deep structures of the nervous system, with comparative safety, without unpleasant side reactions, and with a minimum of exogenous psychological measures. He reported clinical improvement in psychoneuroses in each of four reaction patterns: (a) wherein the objective and subjective evidences of reaction were minimal or absent, (b) wherein there was consistent direct abreaction, fragmented or total, of nuclear psychotraumatic affective and conative constellations, (c) wherein there was consistent indirect abreaction by symbolic dreams, visions, etc., of pathogenic portent, and (d) wherein there occurred between sessions spontaneous recall of "forgotten" pathogenic material, with pertinent insight and self-interpretation of existing symptoms. Active pulmonary tuberculosis, high blood pressure, and organic heart disease were cited as contraindicative to the method.

In November 1948, Meduna[3] elaborated on his preliminary observations, designated the scientific rationale of basic biochemical and physiological approach to neuroticism as a particularized effort to restore a homeostatic balance as conceived of and expressed by Benjamin Rush in 1899 as "a disproportion between excitement and excitability," otherwise commonly called "disease." Meduna attributed the efficacy of carbon dioxide inhalation treatment (as well as other procedures) to an increasing of the threshold of stimulation of the brain against inside and outside stimuli, and cited as advantageous the elimination, thereby, of the necessity of symbolical (i.e., psychological) approach in the treatment of the psychoneurotic. He also reported reactions to carbon dioxide therapy of wider qualitative and quantitative scope; that 20,000 treatments were attended by safety and convenience; that, he reiterated, this treatment is of no permanent help in any psychosis.

Among other publications that have come to hand is that of Wilcox[5] who, after 2,000 odd applications, reported definite advantages in the adding to the method of more multiphasic and conventional approaches in which the psychological component of psychotherapy was maintained in a predominating and (we inferred) an antecedent position. Wilcox modified the manner of administration to facilitate a quick narcosis and a reliance on a retrograde appearance of the reaction-patterns similar to the behavior of a subject reacting from a general anaesthetic. He struck a more optimistic note than Meduna and Loevenhart regarding results in psychotic subjects, especially by the compliment-

ing of the method with electric shock therapy.

The range of speculation that this particular treatment opens up is exemplified by the viewpoint of Kindwall *et al*[6] who view their application and results of the technique in the treatment of the neuroses, as comparable to a "brief, elective, controllable, toxic psychosis."

Discussion

This author's personal experience with Carbon Dioxide Inhalation Therapy in the field of the neuroticisms, concurs generally with those of Doctor Meduna as far as the observed effect of the gas upon the subject is concerned. We do not entirely concur with the theoretical explanations advanced, some of which have been briefly described above. This compendium does not accurately reflect the scientific sincerity and ability such theoretical explanations represent and a review of the sources is therefore suggested. Meduna's initial application of the technique to the exclusion as far as possible of factors predominantly psychological, cannot be commended too highly from a research standpoint, since the purity of his initial conclusions in the field of essentially biological effects, cannot be well contested.

From personal experience with the method as well as perusal of the literature on this and related subjects this author is convinced that Carbon Dioxide Inhalation Therapy's clinical facilitation is a side-result of a pharmacological reaction that is essentially anaesthetic; and regrets the necessity of such a generalization. By definition, general anaesthesia includes the alterations not only of all modalities of sensation but also of consciousness. It modulates, to repeat, but does not eliminate consciousness. This author views consciousness as a phenomenon in itself difficult of analysis to the point of intangency; and further believes that only the over-familiar usage of the term has brought about an over-estimation of any value it in itself may possess as a criterion in its field; and finally, that except in a loosely descriptive utility, the term as far as its antithesis is concerned, (namely, *un*consciousness), is at least in the sphere of the "living," a troublesome, misnamed myth. In this connection he wishes to emphasize that sleep is (psychiatrically) not "unconsciousness."

We believe that the observable reactions of carbon dioxide as an anaesthetic is essentially paralytic and dyscratic rather than stimulative in its immediate physical effects. In common with other concepts of anaesthetic pharmacology, its action is irregularly descending, affecting in rough order, (a) parts of the cortex, (b) all of the cortex, (c) the basil ganglia and subcortical structures, (d) the cerebellum, (e) the sensory cord, (f) the motor cord, and (g) the medulla. We believe that carbon dioxide, as an anaesthetic, has, like other anaesthetics, extraneous side-actions peculiar to its pharmacological texture. Consequently these side-reactions are manifested in sensory, motor, psychosensory, and psychomotor manifestations all roughly predictable. Finally, carbon dioxide may be expected to differ from the other strictly exogenous agents by the fact that it is in itself a powerful physiological agent in the autoregulation of intracranial metabolism.[13-14]

To be more specific this author prefers to attribute the therapeutic efficiency of carbon dioxide inhalation and absorption to retrogressive, functional suppression (in reverse phylo-genetic order) of those cerebral structures of specific gnosi-discriminative utility. It may be further pointed out that, while the withdrawal or release mechanism is in reversed phylo-genetic order (biologically considered), the resulting differential in observable psychologic function is auto-genetically based. This concept is closely allied to the "personal equasion" of everyday language. That cortical inhibitions (so-called) do interfere with freedom of association, is pretty generally conceded.[14,15] We believe the term "analytical cortex" to be hypothetically consistent to our observations but only if it is consistently kept in mind the anthropological fact that "analysis" may be either "correct" analysis or "incorrect" analysis, and certainly, in the everyday actions of life (wherein the super ego functions) it is apt to be "imperfect" analysis.

A generally anaesthetized individual is one partially or wholly deprived of the awake-function of the "analytical cortex"; so is a person normally asleep and this point will be returned to later. We believe that the dynamic concept of personality would hypothesize that an individual deprived, in whole or in part, of his "analytical cortex" (which,

by the way, may or may not have correctly interpreted its environment!) is, in the case of an anaesthetic, still operating on an internal integrative[16] basis while in a state of temporary but definitely altered total personality.

The concept of a dynamic personality would further hypothesize that decisive changes in the personality may be effected in such conditions of temporary alteration and conceivably such changes may be integratively preferred, may be lasting, and may be resistive to change. This change would be expected to manifest itself clinically as pointedly different behavior following such application. Actually such a mechanism is compatible with clinical observation. Repeated temporary removal of cortical influence certainly permits reassociation and strengthening by reenforcement, in accord with the principles conventionally accepted as indigenous to psychologic learning and unlearning.

Finally, we wish to stress the psychobiologic action of carbon dioxide and other anaesthetics in their relation to natural sleep, the therapeutic value of which has long been evident, and to which Rube' has recently made some pertinent references in regard to the treatment of schizophrenia.[17] It may be pertinent to the matter at hand to call attention to the fact that narcosis (or near-narcosis) is a component of this method and numerous other biopsychologic methods, e.g., insulin, narco-therapy, pentathol, electro-narcosis, ether-narcosis,[18] not to mention that method probably more revealing in this respect than all others—namely, therapeutic hypnosis. During the hypnotic trance the mechanisms under discussion appear oftimes to operate before our very eyes and ears.

In the above respects, it may be again emphasized that sleep, psychiatrically, is not unconsciousness; that sleep-function implies a degree of cortical release, however, is observationally tenable. This is particularly striking when we consider the clinical consequences in terms of kinetic tension, when sleep (and the mechanisms implied above) is interfered with, is circumvented, and is prevented by hyper- and dys-function of the gnosi-discriminative organs above referred to. The impact upon our ideation in regard to the commonly observed neurotic end-reaction that follows this example of "inverse reversibility" seems to this author to be extremely significant and evidential in considering the therapeutic effects of any narcosis whatsoever.

This author considers it emphatically pervasive that proper weight be given to the principle, to the trend, to the mechanism variously referred to in psychologic and psychobiological literature as "homodynamic integration," "homeo-stasis," "internal integration," or what have you. It must be reckoned as an instant-to-instant variable operating in constant relationship to a goal. We believe that this idea is a significant and orienting take-off point in any psychiatric consideration whatsoever. The full import of this defies the imagination, but anything less is, we believe, mere comfortable over-simplification.

Evidence and speculation do not point to consequential specificity in the action of carbon dioxide on nervous tissue. The report of Shorvan and Sargent[18] on the use of ether for like purposes would indicate a physiological basis theoretically similar to that cited in the literature covering inhaled CO_2.

McNiece[19] asserts that in four out of five of his cases non-abreactive to CO_2 inhalation a good recall and abreaction were obtained "with verbalization in the present tense" during the purposely prolonged first stage of ether anaesthesia—a technique which permitted indefinite extention of the seance. With only cursory memory to go on, we suspect that any agent of the "anaesthetic" group whose reaction-pattern is characterized by a prolonged or prolongable "stage of delirium or excitement" as currently understood[13,14] may prove to be as effectual to the purpose as inhaled CO_2. The "typical" delirium of pneumonia appears to be anoxic rather than toxic; the mental aberrations associated with high altitudes have parallel causation. Psychiatric speculation on the neuropathology of such "complications" may prove fruitful.

In the author's first acquaintance with the use of carbon dioxide therapy he, like Meduna, made a rigid attempt to divorce suggestive and educational therapy from the technique, and his observations conform pretty well with those of the inventor. However this initial practice was foregone quite

some time ago, and more and more the method has become incorporated into the meyerian regime under which, generally speaking, the author operates. Recently Meduna[4] reports and speculates upon the physiologic significance of the motor and sensory phenomena during carbon dioxide inhalation applications in a manner which would indicate that the trend of thought in regard to this therapy is bending more to the psychologic inclusion.

What has been said above in regard to the similarity of the properties of carbon dioxide to other agents of anaesthesic character appears to gain strength in an evidential way from the findings and the conclusions of Funkenstein, Greenblatt and Solomon[20] following protractive study of alterations produced by electric shock upon the autonomic nervous system; they conclude that such intracerebral alterations can be brought about by other modes of therapy as well as by spontaneous changes in the patient's psychological picture. In the manner of causation they beg the question, except to say, and we agree, that the psychologic and physiologic seem to be parts of the same process. When the psychologic picture changes the physiologic picture changes, and vice versa. As has been aptly stated[20] they fit "as hand into a glove."

Summary

Medical history indicates that current psychiatric consensus is factually vulnerable to subsequent discoveries. The topic is approached and elaborated in the light of this conservatism.

Narcosis and sleep are, psychiatrically, not identical with unconsciousness which is a paradoxical term expressing a mythical idea inconsistent with that of personality-vitality. Psychological effects of general anaesthetics may be interpreted to support this.

The inhalation of carbon dioxide, consequentially considered, is inhibitive, paralytic, and, broadly speaking, dyscratic rather than stimulative in its pharmacologic action and produces alterative effects amenable to cue-learning guided by "homo-dynamic integration." Probably the therapeutic effects of CO_2 may be achieved by other agents but its relative simplicity, speed, safety, and range-width of applicable psychotherapeutic accompaniment makes it, regardless of theory, a tool of merited psychiatric expectancy.

In the dynamic consideration of the human personality, the physiologic as well as the psychologic components are still obscure in their vital essence but evidentially each is capable of operating as both cause and effect in the vital, "total" drive for "homodynamic integration."

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*Fatal Aplastic Anemia Following Tridione Administration**

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Tridione (3, 5, 5-Trimethyloxalidine —2, 4-dione—Abbott) was introduced as a new anticonvulsant in 1945,[1,2] and has since been enthusiastically received. The majority of clinical studies report good results, with little or no toxicity,[2-7] from the drug, whereas the occurrence of aplastic anemia has not been adequately emphasized.[8-15] The present report adds another case of fatal aplastic anemia to the growing list of Tridione-treated epileptics.

Review of Literature

1. In 1946, Harrison, Johnson and Ayer[13] reported the occurrence of a fatal aplastic anemia in a 16 year old female, who had received Tridione for seven and a half months (1½ grains t.i.d.) and Mesantoin (3-methyl-5, 5-phenyl-ethyl hydantoin—Sandoz) for six months (1½ grains t.i.d.). At the time of the hospital admission a severe pancytopenia was already present. In spite of therapy the patient died on the 38th hospital day. Autopsy revealed practically no functioning marrow.

2. In the same year, MacKay and Gottstein[14] reported a fatal aplastic anemia in a 23 year old female who had been taking Tridione for ten months (three grains three to six times daily). A severe pancytopenia was noted on hospital admission. The patient died on the 13th hospital day. (Three days prior to death, the bone marrow was reported as normal!).

3. Greaves,[12] also in 1946, reported the occurrence of a moderately severe leukopenia with neutropenia (WBC 1,900 with 52 per cent neutrophils) in a 25 year old female after 19 days of Tridione treatment (dosage varying from 5 to 10 grains t.i.d.). Tridione was stopped and eight days later the leukocyte count had risen to 5,000. At this time the drug was resumed in a dosage of five grains twice daily. At the end of another eight days, the leukocyte count was 900 with 13 per cent neutrophils. Tridione was again stopped and one month later the leukocyte count was 4,800 with 68 per cent neutrophils. The red blood cell count and hemoglobin remained normal throughout this period.

4. Davis and Lennox[10] (1947) in a hematologic survey of 137 patients receiving Tridione therapy, found a neutropenia of 1,600 or less in 6.3 per cent and 1,600 to 2,500 in 7 per cent. Thus, of the 137 patients, 13.3 per cent had a neutropenia of 2,500 or less.

5. Perlstein,[15] in 1947, in a study of 136 cases treated with Tridione, mentions that "in several instances we observed white blood counts as low as 3,000."

6. In July 1947, Davidoff[9] reported the results obtained following the administration of Tridione to 42 epileptic patients, 32 of whom had received the drug for more than two months. In 24 patients there was a decrease in the leukocyte count to between 2,000 and 5,000. In 11, it was classified as "more than temporary." In 13 a leukocyte count of below 4,500 was noted. The red blood cell count temporarily diminished in only two patients.

7. In March 1948, Carnicelli and Tedeschi[8] reported a fatal aplastic anemia in a 19 year old female who had been taking Tridione (three grains t.i.d.) for approximately five months. At the time of hospital admission a severe pancytopenia was present. Death occurred on the sixth hospital day. At autopsy, the bone marrow was practically non-existent.

8. In April 1948, Gentry and Hill[11] reported a fatal anemia and leukopenia in a six and a half year old boy who had been taking Tridione for three weeks. The dosage was not known inasmuch as the child had refused the medication from time to time. An anemia and a severe leukopenia without thrombocytopenia were present on admission to the hos-

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pital. In spite of vigorous therapy, death occurred on the 19th hospital day. Sections of bone revealed a scanty marrow.

Report of Case

E.B., a 21 year old white female entered the Cook County Hospital on October 5, 1948 because of continuous vaginal and gingival bleeding of three weeks duration. She had also developed a sore throat and shortly thereafter a sudden loss of hearing in the right ear. She had received three transfusions of blood before entering the hospital.

During the previous three years the patient had had monthly grand mal epileptic seizures, unrelated to the menses and uncontrolled by Dilantin Sodium (sodium diphenyl hydrantoinate). Tridione (12 grains t.i.d.) was instituted as the sole anti-convulsant therapy by her family physician one year before the present illness. After several weeks, however, Benadryl (diphenhydramine hydrochloride—Parke Davis Co.) was prescribed concomitantly (100 mg. t.i.d.) because a generalized skin eruption appeared. Both drugs were given daily until the onset of vaginal and gingival bleeding. At this time they were discontinued and Mebaral (mepho-barbital—Winthrop-Stearns) (1½ grains p.i.d.) was prescribed.

Physical examination on admission to the hospital revealed a well developed though poorly nourished, pale girl. The rectal temperature was 102 degrees F., respirations 20, pulse rate 108 per minute and blood pressure 80/40. Ecchymoses were present throughout. There was dry blood on the lips and the gums were bleeding. An agranulocytic membrane was seen on the gums, and there was a small ulcer with a dirty grey base in the left tonsillar fossa. The heart borders were within normal limits. A grade I systolic murmur was heard at the apex. A_2 was greater than P_2. The lungs were resonant throughout and no rales were heard. Abdominal examination revealed no palpable organs or masses. Vaginal bleeding was constant. Neurological findings were not remarkable.

The red blood cell count and hemoglobin were 2.35 million and 44 per cent (6.8 gm.) respectively. The white blood cell count was 2,450 with 2 per cent neutrophils, 1 per cent monocytes, and 97 per cent lymphocytes. The platelet count was 31,000. Bleeding time was over 15 minutes. Urinalysis was negative. Two blood cultures yielded no growth.

No marrow was aspirated from either the sternum or iliac crest in spite of repeated attempts.

Treatment consisted of numerous transfusions of fresh and stored blood and penicillin. Toluidine blue, 100 mgm. in 500 cc. of isotonic saline, was given intravenously on three occasions with no remarkable results. Rutin and folic acid were given daily. Neither ergotrate nor testosterone had any effect on the vaginal bleeding.

Repeated blood studies revealed findings similar to those on admission. Bleeding continued orally and vaginally, and finally rectally. Death occurred on the 28th hospital day. Permission was denied for post-mortem examination.

Discussion

It is unfortunate that the heralding of a new drug is frequently unaccompanied by adequate warning as to its dangers. Sufficient evidence is now available to incriminate Tridione as a potent "myelo-cide." The early recognition of marrow depression and immediate discontinuance of the drug make it possible for the marrow to recover, but it seems likely that subsequent administration may have equally, or perhaps even more serious consequences. Once clinical manifestations of aplastic anemia occur, the chances of recovery are most unlikely. Because early recognition is thus made imperative, the status of the peripheral blood must constantly be checked. By virtue of the great disparity in the longevity of the various type cells in the peripheral blood, the platelets (lifetime about 24 hours) should be the best indicators of impaired marrow function, with the granulocytes next in order. The long life of the erythrocyte makes this cell the least valuable and the appearance of an anemia is indicative of a far advanced and probably irreversible process.

A most interesting theoretical question is whether the marrow depression is on a "toxic" or "hypersensitivity" basis. If the former is the case, then dosage, length of administration, and individual susceptibility will play the most important roles. On the other hand, if the basis for marrow damage resides in hypersensitivity, then the factor

of individual sensitivity will play the most significant role, with dosage and duration of administration of secondary consequence. This point deserves careful study and available data on patients should make clarification of this question possible.

On the basis of the evidence in the literature, our feeling is that Tridione acts as a "toxic" depressant with actual marrow destruction. The destruction, though ultimately involving all cell types, may damage one or another earlier or more seriously, thus giving rise to either thrombocytopenia or agranulocytosis as a presenting manifestation.

Summary

1. A case of fatal pancytopenia, secondary to aplasia of the marrow consequent to the administration of Tridione, is reported. A brief review of previous references to marrow depression is given.

2. The administration of Tridione must be accompanied by constant vigilance for evidences of marrow depression. The drug should be permanently discontinued at the first sign of such evidence.

3. It is suggested that the action of Tridione, in producing aplasia of the marrow, is that of a "toxic" destructive agent rather than a mediation through "hypersensitivity."

Addendum

Since this report was submitted, several additional untoward experiences with Tridione have been encountered in the literature. Braithwaithe (British Med. J., 1:14, 1948) reported a fatal aplastic anemia in an 11 year old boy who had been taking Tridione for 53 days. Briggs and Emery (Lancet, 1:59, 1949) discussed ten cases of petit mal epilepsy in three of whom the drug had to be stopped because of peripheral neutropenia and marrow pancytopenia. Forster and colleagues (Lancet, 1:516, 1949) reported a fatal aplastic anemia in an 11 year old boy who had been taking Tridione intermittently for about six months.

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Neurological Clinical Pathological Conference

OF THE CINCINNATI GENERAL HOSPITAL

CHARLES D. ARING, M.D., Editor

CASE NO. 202584

Presentation

A colored man, a retired porter 65 years of age was admitted to the hospital on October 27, 1945. He had enjoyed good health until that morning at which time he was found on the floor of his room having continuous convulsive movements of the left extremities. He recalled having been awakened early by uncontrollable shaking of his left foot and falling when attempting to get out of bed. He had some vague recollection of a severe frontal headache. The past history failed to contribute understanding to the illness. He had been under medical surveillance for approximately one year because of arterial hypertension.

Physical examination at the time he entered the ward revealed a stuporous man able to move all extremities. He had received paraldehyde in the receiving ward. He did not respond to noxious stimuli. There was left facial weakness of central type, the ankle jerks and skin reflexes were not obtained. He revived shortly after admission when weakness of the left arm was observed and in addition a more profound left facial weakness. The deep reflexes were hyperactive and there were bilateral extensor responses on plantar stimulation. By October 30, he was alert and all the neurological abnormalities had disappeared. He was discharged to his home November 1, 1945.

On November 27, 1945 the patient was readmitted again having continuous left-sided convulsions. After cessation of seizures there was flaccid left hemiplegia, hypoactive deep reflexes and the plantar responses were extensor bilaterally. The heart was moderately enlarged to the left and a systolic murmur was heard at the apex. A hard, irregular, nodular mass was found this time in the upper pole of the right testicle. Immediately after admission, twitching movements were observed to begin in the left facial muscles, spreading to involve the left upper extremity. They continued for approximately two hours until halted. Throughout his hospital stay he continued to have convulsive seizures at irregular intervals. They varied from discrete muscle twitchings usually involving the left foot, to typical grand mal attacks. Between seizures the patient was drowsy but would respond. His course was progressively worse.

On January 3, 1946 he was drowsy but able to cooperate. The pupils were equal and reacted normally; the retinal arterioles were constricted moderately. There was partial, continuous epilepsy involving the left foot; rhythmic twitchings proceeded at an approximate rate of 65 to 70 per minute and produced pronation and internal rotation of the foot with frequent spread to the quadriceps femoris and internal rotators of the thigh. The left side of the face was weak. When the partial epilepsy ceased, the left extremities were paretic, hypalgesic and hypertonic; the right upper abdominal skin reflex was more active than the left; the plantar responses were flexor.

Although anti-convulsant and anti-luetic therapy was accompanied by decrement in seizures, the course was one of increasing confusion, lethargy and wasting. A deep granulating wound developed on the lateral aspect of the left heel. On February 18 lymphangitis, complicating the heel lesion responded to sulfadiazine. On March 15 the patient was found dead in bed.

At the time of the second admission the temperature was 99.6 degrees F., the respiratory rate 24, the pulse 120, and the blood pressure 230/130. Throughout his hospital stay there was irregular fever as high as 102 degrees F.; the pulse rate varied between 80 and 110; the respiratory rate was maintained with fair constancy at about 22; the blood pressure was usually around 180/95.

Laboratory Data: The blood count, hemoglobin determination, urea nitrogen and blood cultures were normal as was stool examination. Repeated urinalyses were normal except for albumin which varied from none to 3 plus.

Blood serological reactions were positive.

Roentgen examination of the chest, skull, pelvis, scrotum and left foot were made. Abnormalities included a nodular type of peribronchial infiltrate in the lower lobes of the lungs on February 18, spinal bifida of 7th and 8th cervical vertebrae, calcified plaques anteriorly in the falx cerebri and in the dura on the right, and an irregular calcified mass 2 x 2.5 cm. in the right testicle. Electroencephalographic studies revealed mild diffuse abnormality (6 to 10 per second waves), and irregular 3 to 5 per second waves in the right occipital region. The record was suggestive of a focal lesion in the latter area.

The cerebrospinal fluid was always water clear with normal white cell counts; colloidal gold curve and Wassermann reactions were normal. Pressure determination measured in mm. of water were respectively 185, 175, 210, 110, 150 and 155 in six punctures from October 27, 1945 to January 3, 1946. The total proteins in mg. per cent were 46, 46, 44, 150, 360 and 36 during the same period of time. At the neurological conference of January 4, 1946 the protein determinations of 150 and 360 mg. per cent were thought possibly to be technical errors since a determination one week later resulted in the figure of 36 mg. per cent. All these tests were done on crystal clear and colorless fluids, on which Pandy tests were negative.

Differential Diagnosis

Dr. Milton Rosenbaum: I propose that we discuss this case by putting ourselves in the place of the physician who was responsible for the care of the patient.

When first seen this 65-year-old colored man was stuporous and neurological examination revealed slight left-sided findings. The history was that of a sudden catastrophic onset with left-sided convulsions. Past history was negative save for a history of hypertension during the previous year. Physical examination revealed rather severe hypertension with no evidence of cardiac failure. The blood serology was positive and the initial cerebrospinal fluid examination was normal except for an initial pressure of 185 mm. and a total protein of 46 mg. The patient cleared up completely in two or three days.

In our diagnostic thinking at this time we would first consider the disease to be on a vascular basis, either vasospasm or a small hemorrhage associated with hypertensive encephalopathy. Vascular neurosyphilis would also have to be considered despite the negative cerebrospinal fluid, although vascular disease associated with hypertension would seem more likely. However, the cerebrospinal fluid findings would make us a bit uncomfortable since there was no evidence of bleeding, and the pressure was high. We might have a passing thought as to the possibility of a cerebral neoplasm, but the rapid improvement of the patient without any residuals would allow us to safely discharge him with the diagnosis of cerebral vascular disease, probably hypertensive encephalopathy.

A month later the patient was readmitted suffering from focal seizures involving the left side which at times spread into grand mal attacks, and there was also left hemiplegia. The seizures were confined for the most part to the left foot. Such seizures are termed epilepsia partialis continua and practically always signify focal cortical irritation. Despite anti-convulsant and anti-luetic therapy, the focal seizures persisted until the patient died 3½ months later.

The findings on physical examination were essentially unchanged except for a small, irregular, nodular lesion in the right testicle which undoubtedly was overlooked on the first admission.

The cerebrospinal fluid examination done shortly after the second admission revealed an initial pressure of 210 mm. and a total protein of 44 mg. At this time our diagnostic thinking must change. The focal neurological findings (left hemiplegia) plus the Jacksonian seizures and epilepsia partialis continua on the left represent precise anatomical localization of a cortical lesion about the right Rolandic area. These findings plus the increased cerebrospinal fluid pressure and the focal EEG abnormalities, favor a space-displacing lesion, and we must now seriously consider the patient to be a brain tumor suspect.

There is a possibility that the cerebral lesion might be metastatic, in view of the findings in the right testicle. However, normal x-ray films of chest, skull and other bone structures are against such a diagnosis. The lesion in the testicle is most likely an old calcified epididymitis. Since all the clinical

evidence favors a lesion irritating the cortex, the type of tumor would most likely be a meningioma.

Although we are now suspecting a brain tumor we must remember that at times an encapsulated intra-cerebral hemorrhage, i.e. one which did not break into the ventricles or subarachnoid space also behaves as a tumor mass. A clinical history favoring cerebral hemorrhage even though the cerebrospinal fluid be clear, and high cerebrospinal fluid pressure must always bring up the possibility of an encapsulated intra-cerebral hemorrhage.

Now at this point in the course of the patient's illness, what should be done? From the protocol it is quite obvious that a diagnosis of cerebral vascular disease was made and this patient was not considered to be a neurosurgical problem so that nothing in the way of more specific diagnostic or therapeutic procedures was done. This was a mistake. I believe the patient was a neurosurgical problem and should have had either air studies (ventriculography) or been explored directly because the clinical signs and symptoms were so focal. Even if the final diagnosis turns out to be cerebral vascular disease, the patient deserved exploration. At times we become too anxious and overwhelmed about neurosurgical procedures; we must remember that a few burr holes for the purpose of exploration is a relatively benign surgical operation.

Now to a few points that are confusing. How do we account for the normal cerebrospinal fluid pressures on the last three taps? I can't, except to say that occasionally the cerebrospinal fluid pressure becomes normal in the course of a brain tumor indicating that intracranial contents, especially vascular, can allow for the growth. This type of compensation is most often seen in slow growing neoplasms. The two high cerebrospinal fluid protein determinations might represent technical errors, although they might also indicate breakdown of cerebral tissue near the ventricles or subarachnoid space, secondary to vascular changes arising locally in relation to the neoplasm. It might be of some interest to point out that the protein became high as the cerebrospinal fluid pressure became normal.

The continued lethargy and drowsiness are characteristic of cerebral neoplasm. A word might be said concerning the generalized wasting that set in. I doubt if this wasting can be explained by any specific lesion, but most likely reflects the hopeless attitude of the service that accompanies a diagnosis of chronic and irreversible cerebral vascular disease. In all probability this patient was not eating and because of the hopeless diagnosis there was little motivation in those responsible for his hospital care to see that his caloric and fluid intake was adequate. If the diagnosis had been more favorable, the patient would have more likely maintained the continued interest of the ward personnel which would have led to better general care. It may well be that such psychological attitudes in the physician-patient and nurse-patient relationship play just as important a role in wasting in chronic, hopeless disease as does the intrinsic disease itself.

My final diagnosis is benign cerebral neoplasm, meningioma, over the right Rolandic area.

Pathological Discussion

Dr. Murton Shaver: Autopsy in this case was performed 7 hours post-mortem, the brain being removed and fixed in formalin as usual. The brain weighed 1320 grams. The general autopsy findings were not of particular interest aside from the presence of bilateral calcification of the epididymes and some generalized congestion of the viscera.

Plaques of calcification were found in the falx and in the left dural leaf extending a distance of 8 cm. over the left cerebral hemisphere in the parietal region. A lobular encapsulated tumor mass measuring 5 x 6 cm. was found firmly adherent to the dura over the right parietal region. This tumor was adherent to the lateral aspect of the falx as well and extended into the adjacent cerebral hemisphere for a depth of 4.5 cm. The tumor mass was firm in consistency and the cut surface had a fibrous and in some areas granular appearance. No areas of hemorrhage or degeneration were observed.

The brain showed generalized flattening of the convolutions with a normal pattern except in a region where the tissue was indented by the tumor. Here the tumor separated readily from the surrounding tissue. The leptomeninges generally were normal in

appearance except for slight opalescense and thickening over some of the sulci which were generally narrowed. The cortical vessels were not remarkable. There was no definite hippocampal herniation or tentorial notching of the brain stem. The cerebellar tonsils were very prominent and there was a suggestion of a cerebellar pressure cone.

The vessels of the Circle of Willis were grossly normal in appearance and distribution. Coronal sections made through the brain at 1 cm. intervals demonstrated the depression caused by the tumor to extend to within 3 cm. of the roof of the right lateral ventricle. There was some generalized edema of the white matter in the right hemisphere and a slight suggestion of herniation of the right hemisphere across the midline and under the falx in the posterior frontal, and parietal regions. Otherwise the midline structures showed no evidence of displacement and the lateral ventricles were equal in size, the ependymal surfaces having a normal appearance. The ventricles were all approximately normal in size, and free from any gross distortion. Sections through the brain stem and cerebellum failed to reveal any gross abnormalities, aside from a suggestion of a cerebellar pressure cone.

Microscopic sections of blocks of tissue removed from the tumor found in the right parasagittal region showed it to have the characteristic appearance of a meningioma (meningeal fibroblastoma). Sheets of endothelial cells and fibroblastic cells were found, many assuming whorl formation which in some cases contained central deposits of calcium or psammoma bodies. The cells were found to be actively producing collagen in many areas. No mitotic figures were seen. The tumor possessed a well defined fibrous capsule.

Blocks of tissue removed from the right parietal cortex underlying the tumor mass showed generalized vacuolization most marked in the white matter and enlargement of the perivascular and pericellular spaces. The vessels generally were congested and swollen. Small perivascular hemorrhages were found. A few of the vessels showed hyaline changes and a few contained thrombi. There was a patchy loss of nerve cells in the cortex in this region with satellitosis and neuronophagia in the deeper layers of the cortex. There was some increase in glial nuclei through these sections but no areas of glial fibrosis were observed. In some areas there were numerous gamistocytic astrocytes. Patchy areas of demyelinization were noted in the white matter of the right parietal lobe with vacuolated histiocytes scattered in these areas. Microscopic sections through the medulla and pons failed to reveal any significant abnormalities.

Clinical Diagnosis

Hypertensive brain disease with softening in the right parietal lobe.

Dr. Rosenbaum's Diagnosis

Meningioma over the right Rolandic Area.

Anatomical Diagnosis

Parasaggital meningioma (right parietal).

Reactive gliosis due to compression anemia right parietal lobe.

Cerebral edema and congestion.

Calcification of the epididymes.

The Short Fuse

(A NOTE ON THE JAPANESE EX-PRISONER OF WAR AFTER FOUR YEARS)*

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In January 1945, intrepid Rangers blasted the gate from the barbed wire stockade at Cabanatuan to liberate hundreds of American prisoners of war. A few days later, the American Forces stormed Manila and crashed through the walls of old Bilibid Prison. At the same time, thousands of American civilians poured from the ancient corridors of Santo Tomas to precious freedom. Now that four years have passed since their dramatic liberation, one is prompted to speculate on their individual fortunes. What has happened to these people?

One of the gaunt and emaciated skeletons, who passed through the gates of old Bilibid, was heard laughingly to remark, that although free, it was his belief that the Japanese had placed an invisible hand grenade about his neck, set with a very short fuse, and would sooner or later explode in his face. The implications of his facetious remark are obvious. However, the grenade was quickly forgotten. Its emaciated recipient was generously outfitted in clothes he had not seen for three years. His belly was fortified with food equally strange and he was hustled off on a transport to his native shores. There, they were waiting for him. When the gangplank hit the dock, he was swept into the arms of a delirious San Francisco. The lid was off; a half dozen bright campaign ribbons were plastered across his chest, and he was presented the keys to a grateful city. The cheers and cries of welcome thundered in his ears no less than the bombs that had cascaded on Clark Field and Cavite. He was in the chips; and his most whimsical desire was no less than a command. A benevolent and beaming paymaster planked down stacks of green-backs with which he might run to the nearest agency to purchase an ancient automobile at three times its value. On a bench in Golden Gate Park, or while merrily drunk in the gutter on Sena Plaza in old Santa Fe, he may have been relieved of his back-pay by some lady of the evening. Often he attempted to push his luck further at the dice and card tables with men whose fingers had not been stiffened by beri-beri. He may have rushed into an unwise and foolish marriage, or else dizzily attempted to patch up the one that had blown to pieces during his absence. After he had retreated behind his own doors, often as not he was assailed by greedy relatives, assembled for the kill, who after the first maudlin tears proceeded to clean his pockets. The tactics of some of these relatives often made similar procedures practiced by the Japanese look like a game of "peeka-boo."

Following this delirious homecoming, and when the shouting had subsided, there became manifest a malady so characteristic and so frequently encountered among ex-prisoners, that it has become a psychiatric entity. This psychiatric disorder, for lack of a better descriptive term, has been called the Japanese P.O.W. Syndrome. It has been essentially an anxiety reaction of a most severe and chronic nature. So protean are its manifestations, that the disease with its usual psychosomatic coloring, might also be termed the "anxiety rainbow," inasmuch as those so afflicted, manifest the entire spectrum of the anxiety state. The affliction was born out of the agony of Bataan, and the despair that was Corregidor, to be nurtured for three and a half long years in the fertile soil of danger, misery, and starvation. Simmering in a veritable witch's cauldron under the diabolical Japanese, the affliction did not reach its full maturity until transplanted upon the shores of the United States. Here with the added assaults of fortune, both good and bad, it was cultured to its full intensity. Strange and ironical, that many of these former prisoners should leave their broken shackles so far behind, only to put them on once more at their own firesides—the same firesides that they had dreamed of in prison for a thousand and one nights. What then, these shackles worn so long and now fastened

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tighter than ever before? What of the grenade with the short fuse?

Anxiety is nothing new to mankind. It has plagued him since his first appearance on this sphere, bedevilling him in some form or another through each stage of his evolution. Beset in all times by constant threats to his security, both by onslaughts from within his own personality, as well as attacks from an external hostile environment, man struggles and pays a price for that citadel we call mental health. Fear, hatred, suspicion, resentment, hostility, guilt, and myriad other ghosts, long buried and repressed, are constant companions on his long and painful journey.

Anxiety, like the pangs of hunger, were a part of the daily existence of the prisoner. Together with his anxiety state, he had to reckon with the ravages of nutritional disorders, dysentery, malaria, and other tropical disease incident to his imprisonment. The residual of these afflictions was the equipment he brought home with him to face the problems of a post-war adjustment. It has now been four years since his return; for some of them it has not been quite that long. Since repatriation, many have spent long months in hospitals; some are still there; some of them are dead; and the others are struggling with varying degrees of success to achieve happiness and security. Some have in a measure regained their health and have found their place; however, there are altogether too many, who except for their freedom, are but little better off than they were the day of their liberation. The following is the case history of a Japanese ex-prisoner, recently admitted to the neuropsychiatric service, who clearly illustrates the difficulties and frustrations encountered by one man in his attempt to make a satisfactory adjustment. Although the history is not entirely typical of the P.O.W. Syndrome, it is significant:

A 29 year old white male veteran, was admitted to the neuropsychiatric service of Fitzsimons General Hospital as a direct admission by authority of the Veteran's Administration following a suicide attempt, in which he swallowed an unknown quantity of hydrochloric acid. Upon admission, the patient though dishevelled and somewhat distraught, did not appear to be in any immediate danger. He had received emergency treatment by a physician who arrived at the patient's home along with the police. At the initial interview, the patient admitted taking the poison stating that he had been depressed, and that he had made the suicide attempt in the hope that his wife would be moved to feel more kindly toward him. He had also been worried over his health and financial matters. He further indicated that there had been considerable turmoil in his marital situation growing out of difficulties between the patient, his wife and his mother-in-law. Sometime previous to his hospitalization, he stated that he had become involved in an altercation with members of his wife's family that resulted in his being jailed on a charge of disturbing the peace. Following this, the wife instituted divorce proceedings against him. Later, he called on his wife in the hopes of a reconciliation which did not materialize. This led to his attempt at suicide and subsequent hospitalization.

The patient was born in 1919. His mother died shortly after his birth and following the death of his father sometime later he was placed in the care of relatives. There are two older sisters, living and well. He finished high school with a good record and then volunteered for the army in 1939. Following basic training, he was sent to the Philippines where he saw combat on Bataan. He was captured by the Japanese and was held in various prison camps on Luzon until his transfer in October 1944 to Japan. During his imprisonment, he suffered hardships and diseases that were the common lot of all war prisoners. Upon his liberation and return to the United States in 1945, he was given a Certificate of Disability Discharge due to faulty vision, bronchiectasis, and malnutrition. Following discharge, he married and found civilian employment in construction work. Since his return home, he has been most ineffective in his work situation. He over indulged in alcohol, suffered from failing vision, and has been very nervous for months on end. At times he would feel fatigued and depressed, amounting to a state of utter despondency. An evaluation of his mental status following admission was not remarkable other than evidence of anxiety, depression, and feelings of insecurity, as revealed by psychometric studies. The physical

and neurological examination was within normal limits except for a loss of vision due to bilateral primary optic atrophy, with a resulting vision of 20/200 OU. There was also manifest marked constriction of the visual fields with scotomata bilaterally. The patient was given a diagnosis of anxiety reaction, and was placed on modified insulin therapy. He suffered no after effects from the hydrochloric acid that he had swallowed in his suicide attempt, probably because of the dilution of the chemical, the small amount ingested, and the prompt emergency treatment received. He recovered rapidly and was soon discharged after four weeks of hospitalization. His future may be considered to be uncertain at the best.

Discussion

As has been stated above, this is not the typical history of that clinical entity that we have chosen to call the Japanese P.O.W. Syndrome. Certain details in the case history presented here, might prompt one to ask whether or not we were dealing with a basic personality or character disorder, rather than an anxiety reaction. The case is merely given as an illustration of one man's struggle. The typical case of the P.O.W. Syndrome encountered, is that of the well integrated pre-war personality who has been rendered more or less non-effective due to his experiences as a Japanese prisoner and his subsequent reaction to a bewildering post-war world. It may be postulated that men who were well integrated prior to the war have as a rule made the best adjustment. However, hundreds of this class of individuals have suffered from the malady under discussion. The clinical picture in many of these patients is indeed puzzling to the average physician due to the fact that there may be no objective findings of organic disease. It must be considered, that there remains the possibility of obscure pathology as yet uncovered in the individual patient. Many of these individuals upon cursory inspection present nothing unusual. Their complaints are generally all out of proportion to the findings, and in some cases one can only marvel at the paucity of pathology, considering the experiences which they have survived. But, let us not be misled; many prisoners have returned from the Japanese wearing the mask of good health.

No other group of war veterans in the history of our country have been so singled out, and more favored, than the ex-prisoners of the Japanese. They have received every benefit and opportunity within the means of a grateful people. It would seem that after four years, the old hurts would be healed, and troublesome fevers smouldered out and forgotten. But, alas, this is not so. The fuse in the grenade for some, continues to burn shorter. Just what more can be done, or in retrospect, what might have been done, are questions that can not be answered here. Certainly, we are having the painful privilege of observing the end results of the most unique, and the most horrible suffering ever experienced by American soldiers. Much could be learned about them, and what we learn might be useful should there be other times.

The State of New Mexico has probably been more aware of the problem under discussion than any other section of the country. With a concentration of approximately one thousand veterans of Bataan and Corregidor within their borders, and the poignant memories of almost as many more who failed to return, the awareness of the people of that state is most understandable. Although a major portion of these veterans are now drawing disability and other benefits, their welfare remains an increasing responsibility. With the passing of time, and further study, much may be accomplished toward a better understanding of their problems.

Clinical Observation of Use of Sodium Pentothal in Heterogeneous Cases

(A PRELIMINARY STUDY)

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We are presenting here a series of heterogeneous cases in which sodium pentothal in a preliminary study proved of some vague value; and by virtue of these results, we feel that further investigation into the use of the drug may be interesting. Above all, we are cognizant of the fact that the material presented in this paper is not statistically significant. However, the cases may prove of academic interest.

As we have pointed out in a previous manuscript,[1] the chief indication for use of sodium pentothal narcosynthesis is in the anxiety state. Also, we have previously discussed the fact that sodium pentothal narcosynthesis alone cannot serve as therapy in the psychoses.[2] Several authors[3,4] have expressed the value of narcosynthesis in evaluating the clinical analysis of schizophrenic deterioration or degree of remission in the psychoses.

However, we have felt that there is an application in certain instances of psychoses where narcosynthesis may prove to be a valuable factor. First, in the cases where the differential diagnosis is between a neurosis and psychosis, and the symptomatology is rather muddled on conscious questioning, the sodium pentothal interview helps to give a clear, distinct picture of the patient's mental content. Second, following shock therapy in the hospital for an acute psychosis, many patients return to their pattern of living still retaining an underlying tendency toward a neurotic pattern or some anxiety and in these cases post-hospital use of narcosynthesis is quite valuable. In relation to these two types of indications, we have used the sodium pentothal interview successfully in the cases herein presented statistically.

To interpret the statistics, there were seven patients seen in the office in which sodium pentothal aided to make a clear cut diagnosis of psychosis. Of the six cases of schizophrenia, two were the ambulatory type and well, remained under office procedure; four were hospitalized for electric-insulin shock treatment. One case of depression was hospitalized with good results. Of the four post-hospital cases, three depressions and one schizophrenia, following shock treatment in the hospital, showed some anxiety tendencies which were adequately relieved by sodium pentothal narcosynthesis.

Pre-hospital and Office		7 cases
Schizophrenia	6	
Hospital	4	
Ambulatory	2	
Depression	1	
Post-hospital		4 cases
Depression	3	
Schizophrenia	1	

We have also seen some helpful results in two alcoholics, since which time O'Hallaren[5] has written an article on the aid of narcosynthesis in alcoholics. We also attempted to aid a very intractible case of neuro-dermatitis with narcosynthesis with some mild improvement. A case of stuttering showed good improvement under sodium pentothal narcosynthesis. One psychopathic personality with excessive masturbation improved considerably under this therapy, and one drug addict with anxiety showed definite improvement under this treatment.

We must emphasize again that we have presented cases only out of academic interest and by no means imply them to be of statistical significance. However, we do foresee the possibility of the use of narcosynthesis in special circumstances as mentioned above, and feel that a more intensive, exhaustive study would be worthwhile. When such a study is completed, including a larger sample over a longer period of time, the results will be published.

Summary and Conclusions

1) We have presented a preliminary study of the use of sodium pentothal narcosyn-

thesis in a series of heterogeneous cases.

2) Narcosynthesis may be helpful in prehospital psychotics in making the diagnosis or in post-hospital psychotics in the treatment of their anxiety or other neurotic symptoms.

3) There may be some value to narcosynthesis in relation to alcoholism, stuttering, neurodermatitis, or psychopathic personalities to give the patient a better insight into himself and his problems.

4) The cases presented are not of statistical significance, but only of academic interest; and in order to be of any value, further studies must be made of larger samples over a longer period of time.

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Newsnotes

Fellowship at Medical College of Virginia: There is available at the Medical College of Virginia a two-year fellowship in psychiatry, with a salary of $3,000 the first year and $3,600 the second. It carries the condition that the person accepting it must serve two years, for each year of fellowship, in one of the state hospitals in Virginia or one of the outpatient clinics. For further information write to Dr. R. Finley Gayle, Jr., Professional Bldg., 5th and Franklin Sts., Richmond, Va.

Residencies Open: Two approved one-year residencies in neuropsychiatry at Parkland Hospital, Southwestern Medical College, Dallas, Texas, are now available. There is a 32 bed ward service in a teaching hospital. For information write to Department of Neuropsychiatry, 2211 Oak Lawn Avenue, Dallas, Texas.

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1 or 2 tablets as required or 3 on retiring. Bottles of 50, 100 & 500.
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